

REMARKS

Claims 1-5, 8-11, 14, 24, and 29-34 were pending and examined in the March 8, 2007 Office Action. Claims 1, 24, and 32 have been amended in this reply. No new matter has been added. Additionally, a Request for Continued Examination is being filed herewith. Accordingly, claims 1-5, 8-11, 14, 24, and 29-34 will be pending upon entry of this amendment.

Claim 1 has been amended to claim with more particularity the types of collagen in the composition for osteoinduction. Support for this amendment is found in the specification as filed on page 10, lines 23-29, and original claims 14-17.

Claim 24 has been amended to claim with more particularity the type of tissue upon which the claimed method can be practiced. Support for this amendment is found in the specification as filed on page 7, lines 22-23.

Claim 32 has been amended to correct a typographical error. The term “odontoblasts” should have read “odontoblasts.” Support for this amendment is found on page 13, line 4 of the specification as filed.

Rejections under 35 U.S.C. § 112, Second Paragraph-Indefiniteness

The Examiner contends that claim 24 is indefinite for failing to particularly point out and distinctly claim the subject matter which the Applicants regard as their invention. Specifically, he argues that the term “tissue” is not interchangeable with the term “bone” used in the preamble and since “bone, calcifying cartilage, dentin and cementum” is the desired site of bone growth, not tissue growth, the inconsistency leaves the claim unclear.

It is respectfully submitted that claim 24 as amended meets the requirements of 35 U.S.C. § 112, second paragraph. The claim has been amended to cover a method of inducing the growth of mineralized tissue, both in the preamble and in the body. Mineralized tissue includes bone, calcifying cartilage, dentin and cementum, as recited in the claim. *See* specification, page 7, lines

22-26. Thus, claim 24 as currently drafted is not unclear, and meets the requirements of 35 U.S.C. § 112, second paragraph.

Rejections under 35 U.S.C. § 102(b)

The Examiner has maintained his rejection to claims 1-5 and 8-11 under 35 U.S.C. § 102(b) as anticipated by Boskey *et al.* (1989) *The Journal of Physical Chemistry* 93:1628-1633 (hereinafter “Boskey”). Specifically he contends that Boskey’s teaching of a dynamic collagen system comprising synthetic complexed acidic phospholipids comprising calcium chloride, phosphatidylserine, and ammonium phosphate reads on claims 1-5 and 8-11. *See* Office Action dated March 8, 2007, page 5.

It is respectfully submitted that claims 1-5 and 8-11 as amended are not anticipated by Boskey. The Boskey article does not disclose a composition wherein all of the components of the claimed composition are present. Specifically, the gel in the Boskey reference is made of gelatin, and not the specific types of fibrillar collagen now recited in the claim.

Moreover, while rat skin collagen fibers are added to the system in Boskey, they are never *added in combination* with the complexed acidic phospholipids. Boskey, page 1631. Boskey does not disclose or suggest the currently claimed complex comprising a complexed acidic phospholipid, and type I, type II, or type IX collagen.

Thus, Boskey does not anticipate claims 1-5 and 8-11 because it does not teach or suggest every claim limitation. Claims 2-5 and 8-11 depend from claim 1 and contain every limitation of claim 1. Boskey does not anticipate these claims as well.

Rejections under 35 U.S.C. § 103

The Examiner rejects claims 24, and 29-34 under 35 U.S.C. § 103 as obvious over U.S. Patent No. 6,311,690 issued to Jefferies (“Jefferies”) in view of U.S. Patent No. 4,578,384 issued to Hollinger (“Hollinger”). Specifically, the Examiner contends that Jefferies teaches a collagen-

calcium conjugate or a reconstituted collagen and acidic phospholipid conjugate that is useful in inducing bone growth. The Examiner further states that Jefferies differs from the present invention in the use of polyglycolic acid and the specific dosage amounts. Hollinger is being used as a supplemental reference to demonstrate the use of bicompatible copolymer such as polyglycolic acid and polyactic acid. The dosages, the Examiner contends, are within the skill of the art. Lastly, the Examiner states that the instant claims use different names for the ingredients than in the cited references but that these references are pertinent and relevant because all of the claimed species and their roles are taught in the cited references. "Thus, one would have been motivated to combine these references and make the modifications because they are drawn to the same technical fields ..., and pertinent to the problem which applicant concerns about." See Office Action dated March 8, 2007, pages 7-9.

This rejection is respectfully traversed.

In order to establish *prima facie* obviousness, the Examiner can show: (1) the references alone or in combination teach or suggest all of the claim limitations; (2) some suggestion and/or motivation in the references or the general knowledge of the art to modify or combine the references; and (3) a reasonable expectation of success. Moreover, there must be an explicit showing of an apparent reason that would have lead a person of skill in the art to combine the teachings of multiple patents to arrive at the claimed invention. *KSR Int'l Co. v. Teleflex Inc.*, Slip Opinion No. 04-1350 (U.S. April 30, 2007), at 14. The Examiner has not done this here.

The teachings of the two references alone or in combination do not teach or suggest every limitation of the claims. As fully shown in the Amendment filed December 11, 2006, Jefferies does not teach or suggest all of the limitations of claims 24, as well as 29-34. Jefferies does not teach or suggest a complexed-acidic-phospholipid-collagen complex comprising calcium, phospholipids, inorganic phosphate, and collagen. This limitation is found in independent claim 24, and dependent claims 29-34. Jefferies discloses a process for inducing bone growth comprising collagen and demineralized bone particles and in one example notes that the collagen matrix can be strengthened with acidic phospholipids. See Jefferies, Example 12. However, Jefferies does not disclose a

complexed acidic phospholipid comprising calcium, phospholipids, and inorganic phosphate. The secondary reference, Hollinger, does not disclose or suggest this missing limitation. Thus, the references either alone or in combination do not teach or suggest all of the claim limitations.

Furthermore, there would have been no motivation to combine the teachings of these two references because Hollinger teaches away from Jefferies. *See KSR*, slip op. at 12. Jefferies teaches the use of collagen and demineralized bone particles for bone repair. Hollinger teaches a material consisting of a combination of proteolipid and biodegradable, biocompatible copolymer for the healing of osseous tissue. Hollinger further discloses that this “represents a significant improvement over conventional materials” such as collagen and bone derivatives, the materials used in Jefferies. *See Hollinger*, column 2, lines 38-50. One of the disadvantages of these materials, according to Hollinger, is an unwanted immunologic response. *Id.* at column 4, lines 12-20. In view of this teaching in Hollinger, there would have been no motivation to combine the teachings of these two references as this patent teaches away from Jefferies because Jefferies uses the materials, *e.g.*, collagen and bone particles, that promote unwanted immune responses, and over which Hollinger “represents a significant improvement.” *See In re Lundsford*, 148 U.S.P.Q. 721, 726 (CCPA 1966). Given that Hollinger states that the materials used in Jefferies would be undesirable and likely cause an unwanted immune reaction, one of skill in the art would not look to combine the teachings of the two references as Hollinger suggests that the result of combining the two would not achieve a desirable result. *See Tec Air Inc. v. Denos Mfg. Mich., Inc.*, 192 F.3d 1353, 1360 (Fed. Cir. 1998).

Indeed, the Examiner’s own citation in support of his assertion actually teaches away from combining the material disclosed in Hollinger with the material disclosed in Jefferies. *See Office Action* dated March 8, 2007, page 7-8; Hollinger, column 14, lines 28-32 (“The results of applicant’s evaluation indicate that copolymer-proteolipid implant material was very successful at stimulating the early phases of bone repair and that it can be used *as an unexpectedly superior alternative to the agents commonly employed for bone repair and reconstruction.*” (emphasis added)). The Examiner has not explicitly shown that there would have been a suggestion and/or a motivation to combine the teachings of these two references. Thus, the presently claimed invention

is not obvious in view of Jefferies and Hollinger because when “the prior art teaches away from combining certain known elements, discovery of a successful means of combining them is more likely nonobvious.” *KSR*, slip op. at 12 citing *U.S. v. Adams*, 383 U.S. 39, 51-52 (1966).

Even if assuming *arguendo* that one of skill in the art would have combined the teachings of these two patents, there would have been no reasonable expectation of success in achieving the claimed invention, *i.e.*, the claimed invention “is more than the predictable use of prior art elements.” *KSR*, slip op. at 13. As shown above, Hollinger leads a person of skill in the art to the contrary conclusion, *i.e.*, that materials such as collagen are immunogenic and should be avoided. This is opposite to the present claims. Thus, one of skill in the art would not have reasonably expected to achieve the presently claimed invention by combining the teachings of these two references.

The Examiner also contends that while Jefferies differs from the present claimed in the specific dosage amounts, it would be within the skill of the art to determine the dosages covered in claims 33 and 34 from Jefferies without undue experimentation. It is respectfully submitted that this assumption is incorrect.

As fully discussed above, Jefferies does not disclose the method of claim 24 for inducing the growth of bone by applying an effective growth stimulating amount of a complexed-acidic-phospholipid-collagen composite, wherein the complex comprises calcium, phospholipids, inorganic phosphate, and collagen. Jefferies alone cannot suggest the amounts of complex to administer when Jefferies does not disclose or suggest the claimed complex to be administered. Moreover, there would have been no motivation to modify Jefferies to obtain the claimed dosages because there is no teaching of the composite to be administered. Additionally, because there is no disclosure or suggestion of the specifically claimed complex, it would not have been routine or predictable for a person of skill in the art to determine the amount of composite to be administered from Jefferies and a person of skill in the art would not have had a reasonable expectation of success in achieving the claimed invention based upon the disclosure of Jefferies alone. Thus, claims 33 and 34 are not obvious.

It is also respectfully submitted that the Examiner should consider objective evidence of unexpected results and advantages of the presently claimed invention over the prior art compositions for osteoinduction. *See In re Rouffet*, 149 F.3d 1350, 1355 (Fed. Cir. 1998). These include lack of rejection of implant material, consistent bone growth across the region in need of growth without the disadvantages of rapid degradation of the composite material, cost-effectiveness, greater osteoinduction than collagen alone and/or in combination of non-stable peptides, and the lack of denaturation during standard sterilization procedures. *See* specification at page 6, lines 27 - page 7, line 2 and page 14, line 28 - page 5, line 10. It should be noted that the first listed advantage, the lack of rejection, is especially surprising and unpredictable in view of the teachings of Hollinger regarding the unwanted immune response of natural materials, such as collagen.

Since the Examiner has failed to prove any of the three criteria for proving *prima facie* obviousness of claims 24 and 29-34 over Jefferies in view of Hollinger, these claims are not obvious and the rejection should be withdrawn.

It is duly noted that claim 14 appears to be free of any prior art or rejections under 35 U.S.C. § 112.

CONCLUSION

In view of the above amendments and remarks, it is respectfully submitted that the pending claims are now in condition for allowance and such action is earnestly solicited. If the Examiner believes that a telephone conversation would help advance the prosecution of this case, the Examiner is respectfully requested to call the undersigned attorney at (212) 527-7631. The Examiner is hereby authorized to charge any additional fees associated with this response to our Deposit Account No. 04-0100.

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Respectfully submitted,

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